

Ovarian tumors in cattle: Case reports

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Abstract. This study aimed to identify bovine ovarian tumors in a local abattoir in Algeria. Histopathological and hormonal evaluations were performed to characterize the type of ovarian tumor and to determine which hormone was secreted by the animal. The obtained data after microscopic examination of ovarian tumor tissues indicated that in two cases it was granulosa cell tumor (GCT). The first GCT showed a trabecular pattern with many metastases. The second GCT showed microfollicular pattern and Call Exner Bodies which confirmed the benign aspect of this neoplasm. The third tumor was Sertoli-Leydig cell tumor. In this case, the neoplasm contained tubules lined by Sertoli cells and interstitial clusters of Leydig cells. The last identified tumor was a simple cystadenoma with multilocular aspect. The liquid contained in the two GCT showed high levels of progesterone while estrogen and testosterone concentrations were low. In contrast, cystadenoma was without noticeable functional activity. In conclusion, this study reports four ovarian tumors in cows with different patterns. To our knowledge, this is likely the first report of Sertoli-Leydig cell tumor of ovary in cows.

Key Words: Ovarian tumor, cow, GCT, cystadenoma, Sertoli-Leydig cell tumor.

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Introduction

Ovarian tumors are common in domestic animals but they are not frequent in cows (Švara et al 2009; DesCôteaux et al 1989). In 20913 routine transrectal palpations, their incidence was less than 0.5%. In another study of 302 bovine tumors, 7% affected the genital tract, including ovaries in 4.3% of the cases (DesCôteaux et al 1989). Ovarian tumors fall generally into three broad categories: surface epithelial tumors, sex cord-gonadostromal tumors, and germ cell tumors (Yener et al 2004). Sex cord-stromal tumors are the most common ovarian neoplasms in cattle (Zachary and Haliburton 1983; Norris et al 1969). These tumors are derived from, or mimic in their growth patterns, constituents of specialized gonadal stroma: cortical and medullary stromal cells, granulosa cells, and theca interna cells of the follicular apparatus (Norris et al 1969). Two types of sex cord tumors derived from granulosa cells have been identified: one composed of typical granulosa cells and the other composed of cells with histologic features similar to Sertoli cells (Zachary and Haliburton 1983). Sex cord-stromal tumors may produce steroid hormones that may result in either nymphomaniac or virilizing effects on the animal (Zachary and Haliburton 1983; Nielsen et al 1976).

The aim of this study was to identify the different types of bovine ovarian tumors existing in an Algerian local abattoir. In addition, to establish a better characterization of these tumors, morphopathological exams and hormonal tests were also performed.

Materials and methods

Samples were obtained during routine inspection from Holstein cows proposed to be slaughtered in an abattoir (El-Harrach, Algiers, Algeria). There is no information about the reproductive history and the age of the cows. After macroscopic examination of the ovaries, oviducts, uterus and vagina of each animal, selected tissues of the genital tract were fixed in 10% buffered formalin and embedded in paraffin wax. During the dissection of the ovaries, the liquid contained in ovarian tumors was aspirated and stored separately at -20°C till analysis.

Microscopic examination of the fixed tissues was carried out at the pathological anatomy laboratories of the NHSV (National High School of Veterinary, Algiers, Algeria) and of Douira Hospital (Algiers, Algeria). Sections cut at $3\mu\text{m}$ thickness were stained with Hematoxylin and Eosin (H&E), and evaluated under a light microscope.

Concentration of progesterone, estradiol 17β and testosterone were assessed by Radio Immuno Assay (RIA) using commercial kits, Immunotech (A Beckman Coulter Company, France). The assay sensitivity was $< 6\text{pg/ml}$ for estradiol 17β , 0.18 pg/ml for testosterone and 0.05 ng/ml for progesterone.

Statistical analysis was conducted using the STATISTICA software (Version 10, Stat Soft France, 2003). Statistical differences in the concentrations of hormonal parameters between ovarian tumors were compared using t-test. Statistical significance was accepted at $P < 0.05$.

Results and discussion

Microscopic examination of ovarian tumor tissues indicated that in two cases it was granulosa cell tumor (TCG). These tumors represent the most common ovarian neoplasms in cows, being usually benign (Sartin *et al* 1996). However, granulosa cell tumors are considered more malignant in cows than in mares (Švara *et al* 2009). Metastases were usually reported to be located in the liver, omentum, cranial lymphnodes, kidneys, adrenal glands, intestines, peritoneum, and various abdominal and thoracic lymph nodes (Norris *et al* 1969). In most reported cases in cows, these tumors are unilateral, with ovoid or spherical shape, usually being encapsulated and limited to the ovary. Color is yellow-gray, with red bands and cysts that have a watery, red-brown or yellow content (Nielsen *et al* 1976). The neoplastic granulosa cells that resemble the granulosa cells of the follicle are most frequently arranged in micro- and macrofollicular, insular, trabecular, and diffuse patterns. A combination of different patterns is often expressed in single tumors (Švara *et al* 2009). In the present study, the first granulosa cell tumor (GCT1) was revealed on the left ovary, 5x4.2x3.5 cm in size, showing necrotic and hemorrhagic foci after incision (Figure 1). Microscopically, this tumor showed a trabecular pattern. Cells were arranged in nests and bands surrounded by septa of connective tissue. Neoplastic cells had basophilic round or ovoid nucleus in incised appearance with one or more nucleoli. The cytoplasm had poorly delineated borders (Figure 2). The finding of cellular anaplasia, necrosis and haemorrhages areas, and vascular invasion by tumour cells were in agreement with previously described characteristics of malignant sex-cord stromal tumours, although mitotic figures were rare (Švara *et al* 2009). In our case, GCT1 showed numerous metastases in the mediastinal and iliacal lymph nodes.

The second granulosa cells tumor (GCT2) is a large formation of 17x14x12cm in size, on the left ovary, cystized, encapsulated and brownish (Figure 3). Histologically, this tumor presented microfollicular architecture with cribriform aspect (Figure 4). The lumen contained eosinophilic secretions bordered by small, round, basophilic monomorphic neoplastic cells in a rosette arrangement 'Call Exner Bodies'. The presence of these bodies is an useful tool for diagnostic. They are most often in the microfollicular pattern (Švara *et al* 2009) and particularly occur in small benign tumors (Nielsen *et al* 1976). This pattern of differentiation is frequently observed in early stages of bovine neoplasms, but is less common in other species and in large tumors (Švara *et al* 2009). According to the classification of Human ovarian tumors, GCT with microfollicular or trabecular pattern is part of 'well differentiated GCT' (Roth 2006).

The third ovarian tumor identified was Sertoli-Leydig cells tumor, commonly known as «Arrhenoblastoma» (Norris *et al* 1969). As far as we could determine, these tumors have never been described previously in cows but only in women, mare, cat and camel (Roth 2006; Shawky *et al* 2004). They are grouped, together with the GCT, under the term 'Stromal tumors', as reported by Norris *et al* (1969). These tumors occur in older cows, but are found sometimes in animals less than 4 years old or even in calves. There is no breed predilection in any species (Zachary and Haliburton 1983). According to Roth (2006), human Sertoli-Leydig cells tumor is composed of variable proportions of Sertoli cells, Leydig cells, and in the case of intermediate and



Figure 1. Granulosa cells tumor 1. Bar, 1 cm

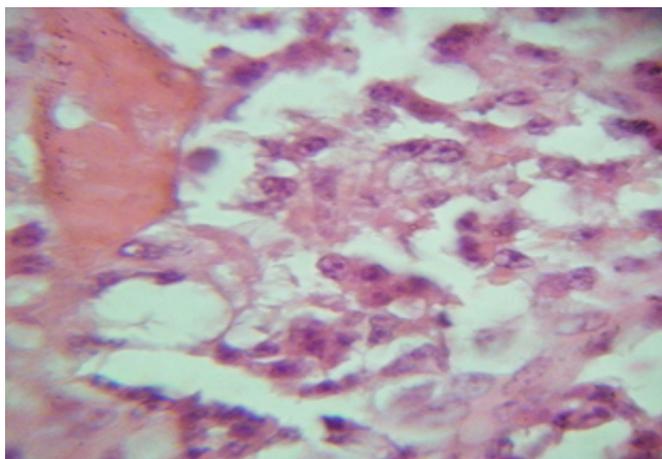


Figure 2. Microscopic aspect of GCT1 (diffuse pattern with necrotic and hemorrhagic foci). Bar, 15 µm

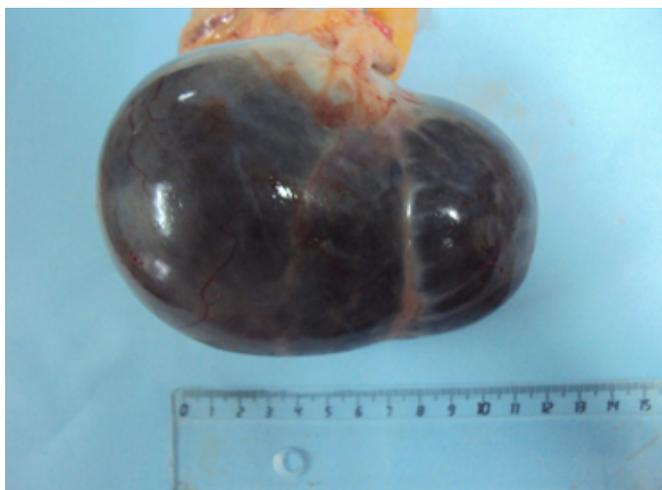


Figure 3. Granulosa cells tumor 2. Bar, 1 cm

poorly differentiated neoplasms, primitive gonadal stroma, rete epithelial cells, and/or heterologous elements. Four subtypes are described that have differing biological behavior: well differentiated, of intermediate differentiation, poorly differentiated, and retiform. In this case, the neoplasm contained tubules lined by Sertoli cells and interstitial clusters of Leydig cells. Gross appearance of the tumor is unilateral (affecting the right ovary), large (20x16x12cm), firm, solid, with a necrotic focus at the periphery (Figure 5). Microscopically, this tumor consists of two

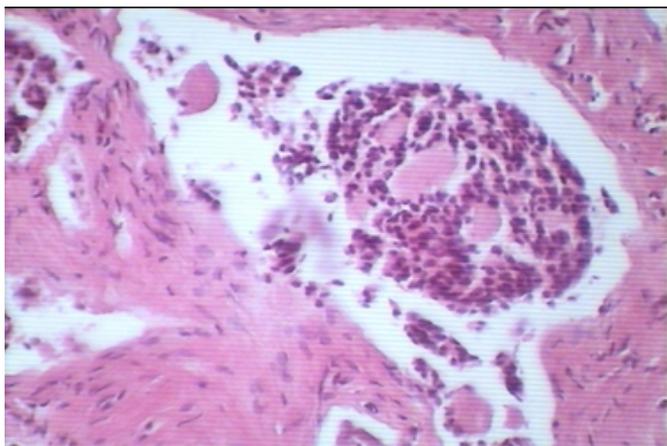


Figure 4. Histological aspect of GCT2. Microfollicular pattern with cribriform aspect and call exner bodies. Bar, 20 μ m

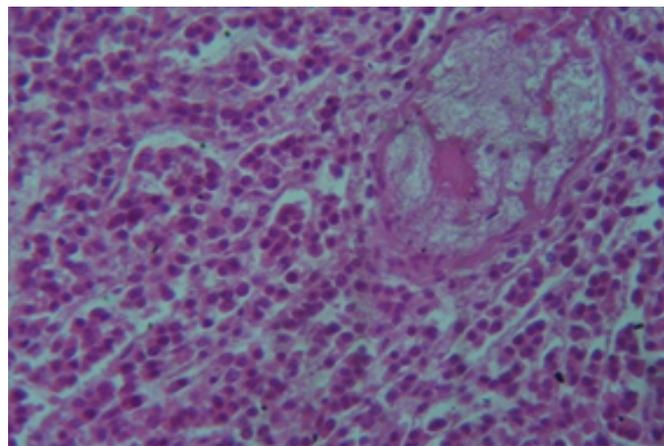


Figure 7. Leydig cells with abundant eosinophilic pink cytoplasm. Bar, 20 μ m



Figure 5. Sertoli-Leydig cells tumor. Bar, 1 cm

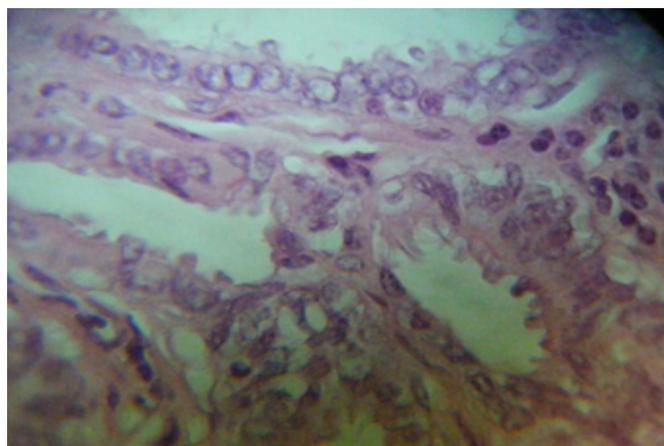


Figure 8. Ovarian cystadenoma presenting multilocular aspect. Bar, 15 μ m

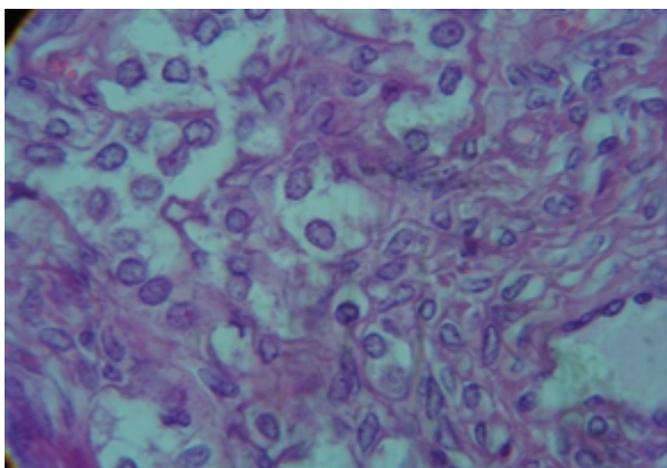


Figure 6. Sertoli cells with pale cytoplasm. Bar, 15 μ m

different cell types: Sertoli cells and Leydig cells. Sertoli cells showed tubular arrangement that grow in a fibrous stroma that contains nests of Leydig type cells. They were usually elongated and arranged in solid clusters. Cytoplasm was frequently pale and vacuolated. Nuclei sit near the basement membrane away from the tubule lumen with vacuolated-appearing chromatin. Mitotic figures were rare (Figure 6). Leydig cells were polygonal pink cells with abundant solid or granular eosinophilic cytoplasm. Nuclei were round with fine chromatin and a small or indistinct nucleolus (Figure 7). Varying amounts of

lipid were presented in the neoplastic cells, as previously described by Norris *et al* 1969.

The last tumor found in this study was cystadenoma. This tumor is uncommon in all domestic animals. It has been reported in the horse, bitch, mare, cat, mostly in adult or aged animals (Yener *et al* 2004; Nielsen *et al* 1976). In the bitch, it occurs together with cystic endometrial hyperplasia, which is why gross and microscopic descriptions are only given for this species (Garcia Iglecias *et al* 1991). There is no breed predisposition. These neoplasms are usually unilateral in the ovary (Moulton 1978). In our case, the left ovary was affected (5.3x4.25x2.8cm in size) and presented a very lobulated surface. It was formed by a connective tissue stroma containing many cysts which showed a clear watery liquid when the ovary was cut. The uterus was normal. Microscopically, the cysts were lined entirely by a single layer of cuboidal to flattened epithelium and nuclei with fine chromatin (Figure 8). Therefore, the tumor could be designed as simple cystadenoma with multilocular aspect, in accordance with other reports (Yener *et al* 2004; Nielsen *et al* 1976). Cells appeared ciliated or with the apical part of the cytoplasm prominent in the lumen delimiting irregular cavities. Mitotic figures were uncommon. This tumor probably arises from the surface epithelium or from underlying epithelium nests in the cortex of the ovary. Rarely, it develops from the rete ovarii (Garcia Iglecias *et al* 1991; Moulton 1978).

Table 1. Hormonal levels in ovarian tumors

	Estradiol 17-β	Progesterone	Testosterone
	(pg/ml)	(ng/ml)	(pg/ml)
GCT1	16	77.78	23.56
GCT2	15.32	120	30.14
Cystadenoma	1.26	32.11	10.04

Hormone assays are necessary in order to relate the histology of the tumor to the type of hormone being produced (Moulton 1978). Table 1 showed the hormonal levels of the liquid aspirated from ovarian tumors. The third tumor (Sertoli-Leydig cells tumor) was excluded because this tumor was solid and didn't contain any liquid. In this study, the liquid contained in GCT2 and GCT1 showed high levels of progesterone, respectively ($P < 0.001$) while estrogen and testosterone concentrations were low ($P > 0.05$). Therefore, we suggest that estrus in these cows was prolonged or absent and the animals were infertile. In contrast, cystadenoma was without noticeable functional activity since this neoplasm showed low hormonal levels in comparison with the two GCT ($P < 0.001$). This result is in agreement with those reported previously in domestic animals (Moulton 1978; Norris et al 1969) and Humans (Yener et al 2004).

In conclusion, the current study reports four ovarian tumors in cows and demonstrates the usefulness of morphopathological exams and hormonal evaluation to determine the characteristics of each tumor. As far as the authors know, this is likely the first report of Sertoli-Leydig cells tumor of ovary in cows.

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